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## TUMOR CELLS MODIFIED TO EXPRESS B7-2 AND B7-3 WITH INCREASED IMMUNOGENICITY AND USES THEREFOR

def 2/2/04 Government Funding

Work described herein was supported under grant awarded by the National Institutes of Health. The U.S. government therefore may have certain rights to this invention.

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Related Applications

This application is a Continuation-in-part of U.S. Serial No. 08/147,773 filed November 3, 1993 entitled "Tumor Cells Modified to Express B7-2 and B7-3 with Increased Immunogenicity and Uses Therefor". The contents of this application is incorporated herein by reference.

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## **Background of the Invention**

Induction of a T lymphocyte response is a critical initial step in a host's immune response. Activation of T cells results in T cell proliferation, cytokine production by T cells and generation of T cell-mediated effector functions. T cell activation requires an antigen-specific signal, often called a primary activation signal, which results from stimulation of a clonally-distributed T cell receptor (hereafter TcR) present on the surface of the T cell. This antigen-specific signal is usually in the form of an antigenic peptide bound either to a major histocompatibility complex (hereafter MHC) class I protein or an MHC class II protein present on the surface of an antigen presenting cell (hereafter APC). CD4+ T cells recognize peptides associated with class II molecules. Class II molecules are found on a limited number of cell types, primarily B cells, monocytes/macrophages and dendritic cells, and, in most cases, present peptides derived from proteins taken up from the extracellular environment. In contrast, CD8+ T cells recognize peptides associated with class I molecules. Class I molecules are found on almost all cell types and, in most cases, present peptides derived from endogenously synthesized proteins. For a review see Germain, R., *Nature* 322, 687-691 (1986).

It has now been established that, in addition to an antigen-specific primary activation signal, T cells also require a second, non-antigen specific, signal to induce full T cell proliferation and/or cytokine production. This phenomenon has been termed costimulation. Mueller, D.L., et al., Annu. Rev. Immunol. 7, 445-480 (1989). Like the antigen-specific signal, the costimulatory signal is triggered by a molecule on the surface of the antigen presenting cell. A costimulatory molecule, the B lymphocyte antigen B7, has been identified on activated B cells and other APCs. Freeman, G.J., et al., J. Immunol. 139, 3260-3267 (1987); Freeman, G.J., et al., J. Immunol. 143, 2714-2722 (1989). Binding of B7 to a ligand

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